

**THAT WHICH IS CLAIMED IS:**

1. A method of assessing cardiac ischemia in a subject to provide a measure of cardiovascular health in that subject, comprising said steps of:

(a) collecting a first RR- interval data set from said subject during a stage of gradually  
5 increasing heart rate;

(b) collecting a second RR- interval data set from said subject during a stage of gradually decreasing heart rate;

(c) separating fluctuations from a slow trend in said first RR- interval data set;

(d) separating fluctuations from a slow trend in said second RR- interval data set;

10 (e) comparing said fluctuations of said first RR- interval data set to said fluctuations of said second RR- interval data set to determine a difference between said fluctuation data sets; and

(f) generating from said comparison of step (e) a measure of cardiac ischemia during stimulation in said subject, wherein a greater difference between said first and second data  
15 sets indicates greater cardiac ischemia and lesser cardiac or cardiovascular health in said subject.

2. The method of claim 1, wherein:

said step (c) of separating fluctuations from at least one slow trend in said first RR-  
20 interval data set includes smoothing said first RR- interval data set to determine at least one slow trend in said first RR-interval data set; and

said step (c) of separating fluctuations from at least one slow trend in said second RR- interval data set includes smoothing said second RR- interval data set to determine at least one slow trend in said second RR-interval data set.

25 3. The method of claim 1, wherein said comparing step (e) is carried out at substantially equal trend values of said RR- intervals.

4. The method of claim 1, wherein said first and second RR- interval data sets are  
30 collected without an intervening rest stage.

5. The method of claim 1, wherein said first and second RR- interval data sets are collected under quasi-stationary conditions.

6. The method of claim 1, wherein said stage of gradually increasing heart rate and said stage of gradually decreasing heart rate are each at least 3 minutes in duration.

5           7. The method of claim 1, wherein said stage of gradually increasing heart rate and said stage of gradually decreasing heart rate are together carried out for a total time of from 6 minutes to 40 minutes.

10           8. The method of claim 1, wherein:  
both said stage of gradually increasing heart rate and said stage of gradually decreasing heart rate are carried out between a peak rate and a minimum rate; and  
said peak rates of both said stage of gradually increasing heart rate and said stage of gradually decreasing heart rate are the same.

15           9. The method of claim 8, wherein:  
said minimum rates of both said stage of gradually increasing heart rate and said stage of gradually decreasing heart rate are substantially the same.

20           10. The method of claim 1, wherein said stage of gradually decreasing heart rate is carried out at at least three different heart-rate stimulation levels.

11. The method of claim 10, wherein said stage of gradually increasing heart rate is carried out at at least three different heart-rate stimulation levels.

25           12. The method of claim 1, wherein said stage of gradually increasing heart rate and said stage of gradually decreasing heart rate are carried out sequentially in time.

13. The method of claim 1, wherein said stage of gradually increasing heart rate and said stage of gradually decreasing heart rate are carried out separately in time.

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14. The method of claim 1, wherein said heart rate during said stage of gradually increasing heart rate does not exceed more than 120 beats per minute.

15. The method of claim 1, wherein said heart rate during said stage of gradually increasing heart rate exceeds 120 beats per minute.

16. The method of claim 1, wherein said first and second RR- interval data sets are  
5 collected by pulse or blood pressure monitoring.

17. The method of claim 1, wherein said comparing step is preceded by the step of generating fluctuation curves for each of said data sets.

10 18. The method of claim 17, wherein said comparing step includes comparing the shapes of said fluctuation curves of each of said data sets.

19. The method of claim 17, wherein said comparing step includes determining a measure of the domain between said fluctuation curves.

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20. The method of claim 19, wherein said comparing step includes a step of connecting said curves with a connecting segment to form a closed domain bounded by said fluctuation curves and said connecting segment.

20 21. The method of claim 20, wherein said comparing step includes determining a measure of the domain bounded by said fluctuation curves and said connecting segment.

22. The method of claim 17, wherein said comparing step includes both comparing the shapes of said fluctuation curves and determining a measure of the domain between said  
25 fluctuation curves.

23. The method of claim 17, further comprising the step of displaying said fluctuation curves.

30 24. The method of claim 1, wherein said separating step (c), said separating step (d) and said comparing step (e) are carried out by:

(i) smoothing said first and second RR- interval data sets to generate first and second slow trend data sets;

(ii) separating fluctuations from said second said slow trend in said first and second data sets to generate first and second fluctuation data sets;

(iii) generating a first fluctuations versus trend curve from said first slow trend data set and said first fluctuation data set;

5 (iv) generating a second fluctuations versus trend curve from said second slow trend data set and said second fluctuation data set;

(v) generating a hysteresis loop from said first fluctuations verses trend curve and said second fluctuations versus trend curve; and

10 (vi) determining a measure of the domain inside said smoothed hysteresis loop to thereby quantify a difference between said fluctuation data sets.

25. The method of claim 25, further comprising the step of :

15 adding a connecting segment between said first and second fluctuations versus trend curve to generate a closed hysteresis loop bounded by said first and second fluctuations versus trend curves and said connecting segment;

and wherein said determining step is carried out by determining a measure of the domain inside said smoothed closed hysteresis loop.

20 26. The method of claim 1, wherein said separating step (c), said separating step (d), and said comparing step (e) are carried out by:

(i) smoothing said first and second RR- interval data sets;

(ii) generating first and second smoothed trend versus time curves from said smoothed first and second RR- interval data sets;

25 (iii) generating first and second cardiac cycle length fluctuations versus time curves by separating fluctuations from slow trends;

(iv) generating an open hysteresis loop having two branches from said first and second trend versus time curves and said first and second fluctuations versus time curves

(v) connecting said branches of said open hysteresis loop to generate a closed hysteresis loop; and then

30 (vi) determining a measure of the domain inside said closed hysteresis loop to thereby quantify a difference between said fluctuation data sets.

27. The method of claim 26, wherein said generating step *(iii)* is followed by the step of fitting said first and second smoothed curves trend versus time curves.

28. The method of claim 26, wherein said generating step *(iv)* is followed by the step  
5 of smoothing said first and second fluctuation versus time curves.

29. The method of claim 1, further comprising the step of:

*(g)* comparing said measure of cardiac ischemia to at least one reference value; and  
then

10 *(h)* generating from said comparison of step *(e)* a quantitative indicium of cardiac ischemia for said subject.

30. The method of claim 29, further comprising the steps of:

*(i)* treating said subject with a cardiovascular therapy; and then

15 *(j)* repeating steps *(a)* through *(f)* to assess the efficacy of said cardiovascular therapy, in which a decrease in the quantitative indicium from before said therapy to after said therapy indicates an improvement in cardiac health in said subject from said cardiovascular therapy.

31. The method of claim 30, wherein said cardiovascular therapy is selected from the  
20 group consisting of aerobic exercise, muscle strength building, change in diet, nutritional supplement, weight loss, stress reduction, smoking cessation, pharmaceutical treatment, surgical treatment, and combinations thereof.

32. A computer system for assessing cardiac ischemia in a subject to provide a  
25 measure of cardiac or cardiovascular health in that subject, said system comprising:

*(a)* means for providing a first RR- interval data set collected from said subject during a stage of gradually increasing heart rate;

*(b)* means for providing a second RR- interval data set from said subject during a stage of gradually decreasing heart rate;

30 *(c)* means for separating fluctuations from slow trends in said first RR- interval data set;

*(d)* means for separating fluctuations from slow trends in said second RR- interval data set;

(e) means for comparing said fluctuations of said first RR- interval data set to said fluctuations of said second RR- interval data set at equal trend values of said RR- interval to determine said difference between said fluctuation data sets;

5 (f) means for generating from said comparison of step (e) a measure of cardiac ischemia during stimulation in said subject, wherein a greater difference between said first and second data sets indicates greater cardiac ischemia and lesser cardiac or cardiovascular health in said subject.

10 33. The system of claim 32, wherein said means (e) for comparing said fluctuations of said first RR- interval data set to said fluctuations of said second RR- interval data set compares said fluctuations at substantially equal trend values of said RR- interval.

34. The system of claim 32, further comprising:

15 (g) means for comparing said measure of cardiac ischemia to at least one reference value; and

(h) means for generating from said comparison of step (e) a quantitative indicium of cardiac ischemia for said subject.

20 35. A computer program product for assessing cardiac ischemia in a subject to provide a measure of cardiac or cardiovascular health in that subject, said computer program product comprising a computer usable storage medium having computer readable program code means embodied in said medium, said computer readable program code means comprising:

25 (a) computer readable program code for comparing a first RR- interval fluctuation data set to a second first RR- interval fluctuation data set to determine said difference between said data sets; and

30 (b) computer readable program code for generating from said code (a) a measure of cardiac ischemia during stimulation in said subject, wherein a greater difference between said first and second fluctuation data sets indicates greater cardiac ischemia and lesser cardiac or cardiovascular health in said subject.

36. The system of claim 35, wherein said computer readable program code for comparing a first RR- interval fluctuation data set to a second RR- interval fluctuation data set compares said fluctuations at substantially equal trend values of said RR- intervals.

5           37. The system of claim 35, further comprising:

          (c) computer readable program code for comparing said measure of cardiac ischemia to at least one reference value; and then

          (d) computer readable program code for generating from said code (e) a quantitative indicium of cardiac ischemia for said subject.